



Platform Therapy for Aging-Related
Injury and Neurodegeneration

Turning Irreversible Into Recoverable

Restoring neurovascular integrity with a first-in-class biologic therapy

May 2026 | Non-Confidential Deck

William D. Schwieterman, M.D.
CEO, Stream Biomedical Inc.
251-377-4828 | wds@streambiomed.com

streambiomedical.com

Non-confidential disclosure

For millions living with neurodegenerative disease,
recovery may finally be within reach.



A GLOBAL HEALTH CRISIS

Neurodegenerative diseases impact tens of millions worldwide and remain one of the greatest unmet needs in medicine.



THE LIMITS OF CURRENT APPROACHES

Current approaches primarily target downstream pathology while leaving the underlying neurovascular dysfunction unresolved.



A DIFFERENT KIND OF THERAPY

Stream Biomedical is developing rLG3, a novel recombinant protein designed to restore brain function through **neurovascular repair**.

Failure of neurovascular repair drives neurodegeneration

Growing evidence shows that dysfunction of the neurovascular unit is a central driver across neurological diseases.



Pericyte loss and vascular instability



Impaired cerebral perfusion



Blood-brain barrier dysfunction



Chronic neuroinflammation
and impaired repair

Over time, breakdown of these systems leaves the brain **unable to maintain or repair itself.**



Neurovascular
Restoration



Vascular Integrity
& Repair



Enhanced Perfusion
& Support



Targeted, Systemic
Neuroregeneration

What if the brain could recover?

Stream is developing a new class of biologics — **vascular matrikines** — designed to restore neurovascular integrity by amplifying endogenous repair signaling.



Restores neurovascular stability and repair
Reinforces the brain's capacity to maintain and heal its own vascular network.



Enhances vascular integrity and neuronal support
Improves perfusion and the microenvironment that neurons depend on.



Targets shared upstream mechanisms
Addresses common drivers of neurodegeneration across multiple diseases.

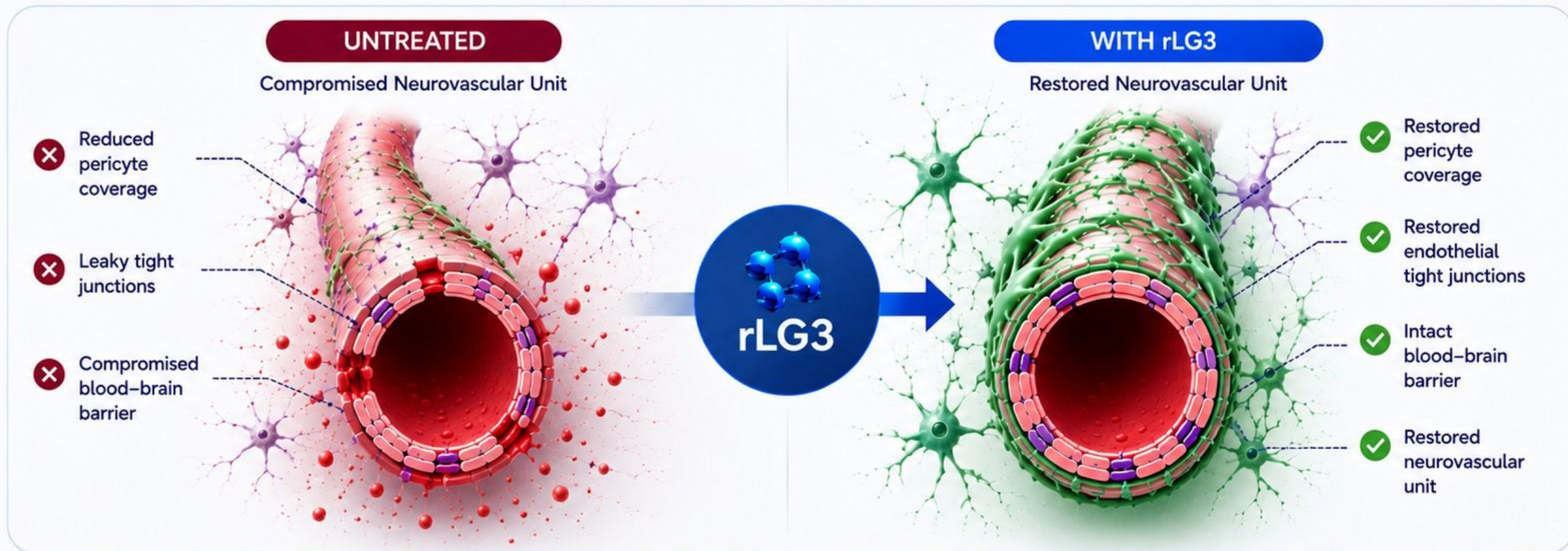


A unified neurovascular approach to neurodegenerative disease.

Introducing rLG3: A First-in-Class Recombinant Biologic

Derived from a Natural Endogenous CNS Repair Protein

rLG3 restores neurovascular integrity and CNS homeostasis following injury by restoring pericyte coverage and endothelial tight junctions.



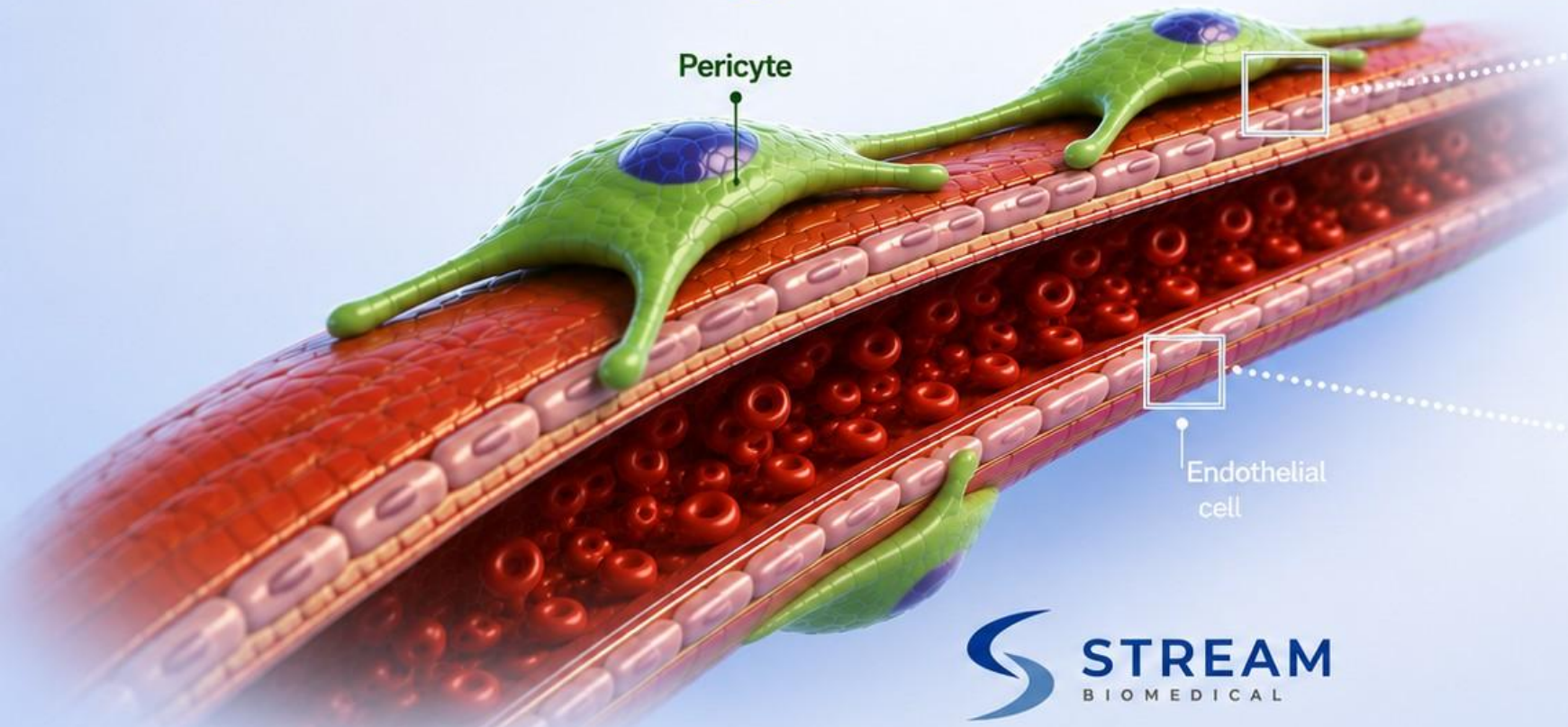
Restoring the brain's own repair mechanisms to protect, heal and restore.

rLG3 restores pericyte coverage by engaging integrin receptors.

rLG3 is a vascular matricine that binds to integrin receptors on pericytes and endothelial cells to promote pericyte recruitment, adhesion, and stabilization on blood vessels.

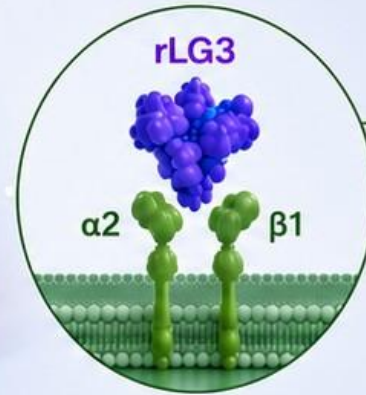


The result: Restored pericyte coverage. Stronger vessels. Healthier brain.



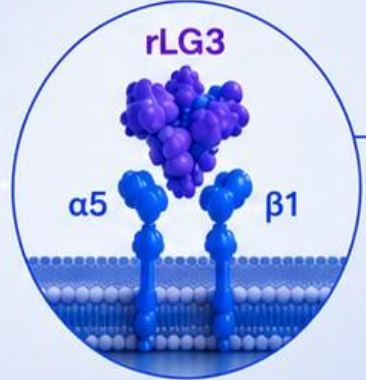
Pericyte

Endothelial cell



rLG3 binds to $\alpha2\beta1$ integrin on pericytes

This interaction promotes pericyte recruitment, adhesion, and stabilization on the vessel wall.



rLG3 binds to $\alpha5\beta1$ integrin on endothelial cells

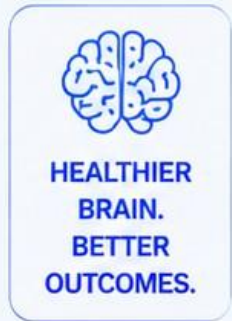
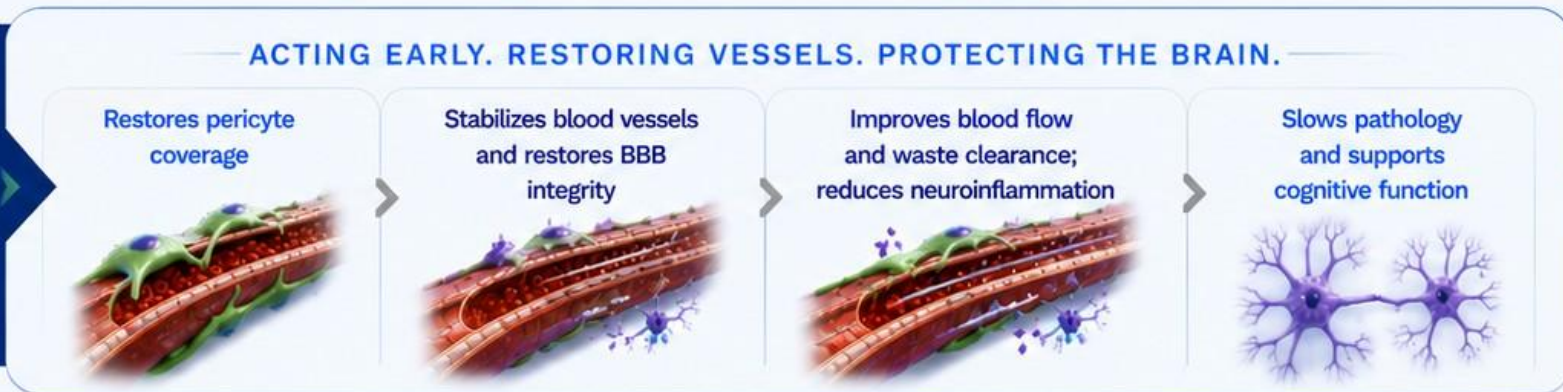
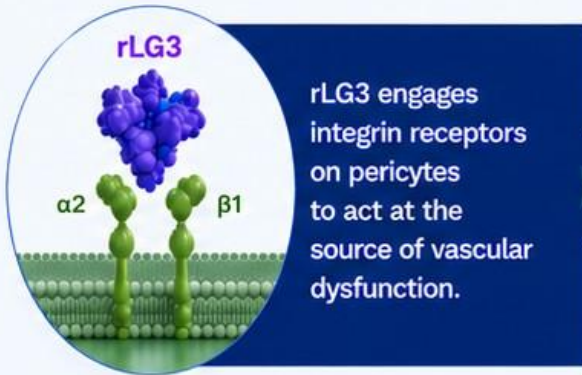
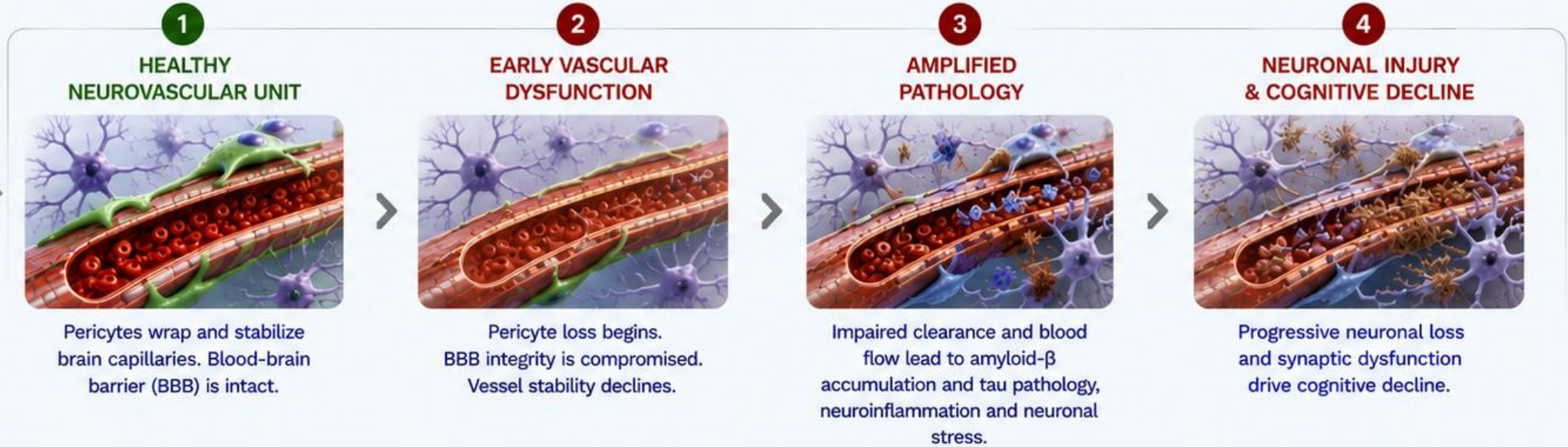
This interaction supports endothelial cell function and vessel integrity.

rLG3 acts **early** to restore the neurovascular foundation

In Alzheimer's disease, vascular dysfunction begins early—driving and accelerating pathology. rLG3 targets the earliest vascular changes to restore pericyte coverage and support a healthy brain.

THE ALZHEIMER'S DISEASE CASCADE

Vascular dysfunction occurs early—often before clinical symptoms.



Why Pericytes Matter: Published Human and Preclinical Data Show Neurovascular Dysfunction Drives Downstream Pathology

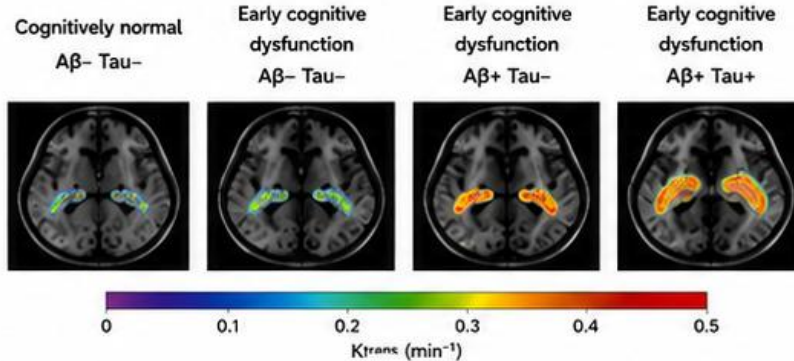
Pericyte injury and BBB breakdown occur early, predict cognitive decline, and cause downstream pathology.

1 HUMAN EVIDENCE

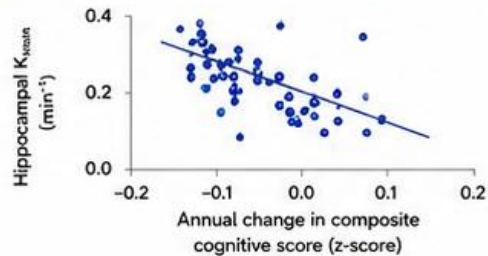
BBB breakdown occurs early and predicts cognitive decline

Nation et al., *Nature Medicine*, 2019

Hippocampal BBB Permeability (DCE-MRI)



BBB leakage is present in early cognitive dysfunction, before substantial amyloid or tau pathology.



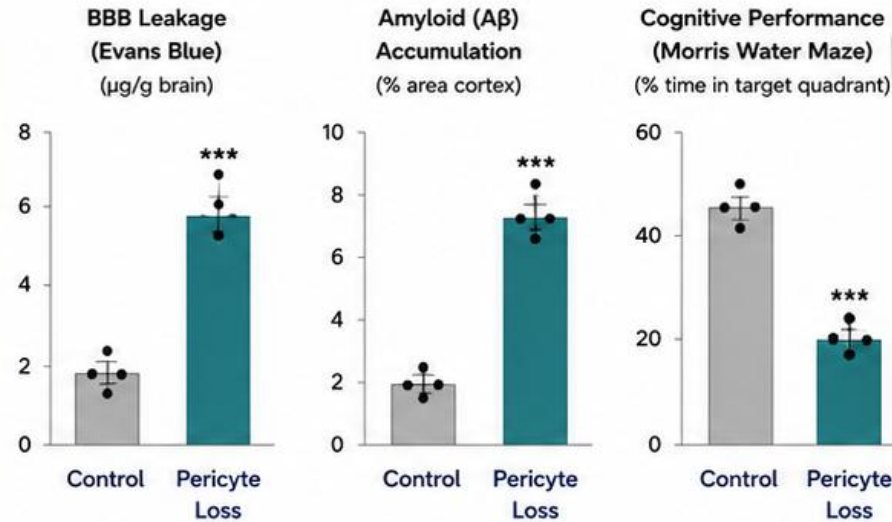
Higher hippocampal BBB permeability independently predicts future cognitive decline ($r = -0.52, p < 0.001$)

2 PRECLINICAL EVIDENCE

Pericyte loss causes BBB breakdown, pathology, and cognitive deficits

Sagare et al., *Neuron*, 2013

Mouse model: Pericyte depletion in APP mice



Pericyte loss is sufficient to drive BBB breakdown, increased amyloid accumulation, and cognitive impairment.

KEY TAKEAWAYS



Occurs Early
BBB dysfunction and pericyte injury are detectable in early cognitive dysfunction, before amyloid or tau accumulation.



Predicts Decline
Neurovascular dysfunction independently predicts future cognitive decline, even after controlling for amyloid and tau.



Drives Pathology
Pericyte loss causes BBB breakdown, increases amyloid accumulation, and leads to cognitive deficits.

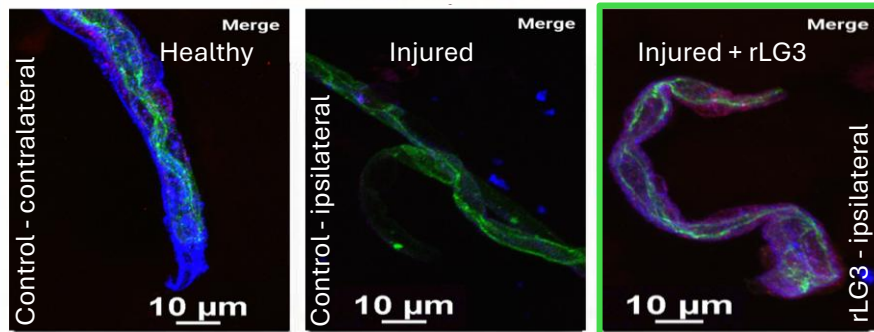


Published human and preclinical studies support pericyte / BBB dysfunction as an upstream driver of neurodegenerative processes.

rLG3 Restores Neurovascular Integrity Driving Amyloid Clearance and Cognitive Improvement

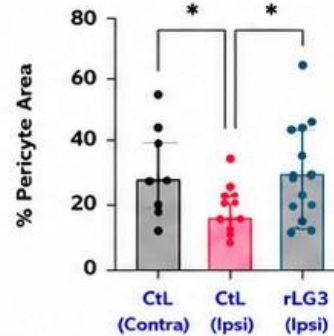
1. Restored Pericyte Coverage of Brain Capillaries

Acute Ischemic Stroke Murine Model



PDGFR-β (Pericyte) Claudin-5 (Endothelial) Lectin (Vessel)

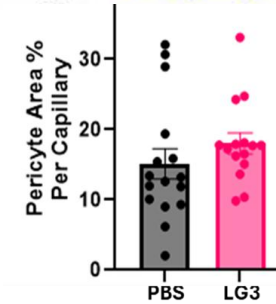
Pericyte Coverage (% Pericyte Area Per Capillary)



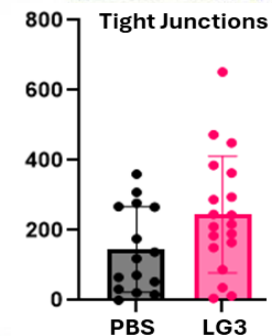
2. Strengthened BBB Integrity

5XFAD Murine Alzheimer's Model

Pericyte Coverage (% Pericyte Area Per Capillary)



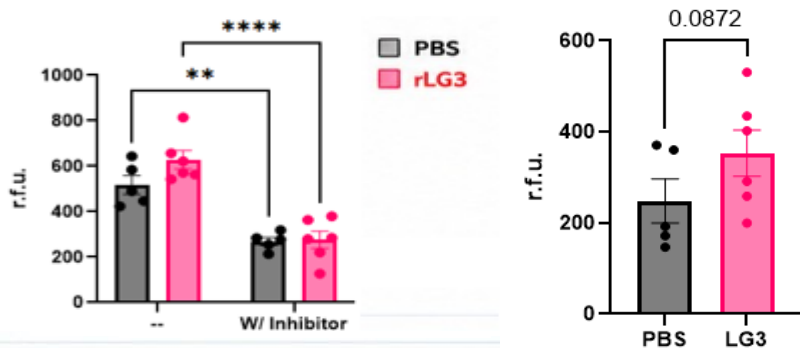
Endothelial Tight Junctions (Claudin-5, r.f.u.)



3. Increased Efflux of Amyloid Protein

db/db mice

Amyloid Efflux in Freshly Isolated Brain Capillaries

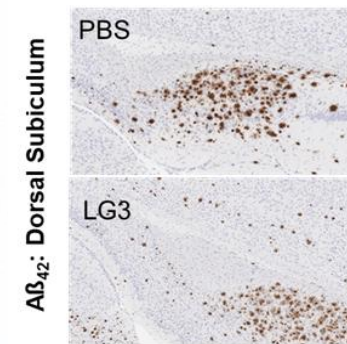


4. Downstream Impact: Reduced Amyloid Pathology

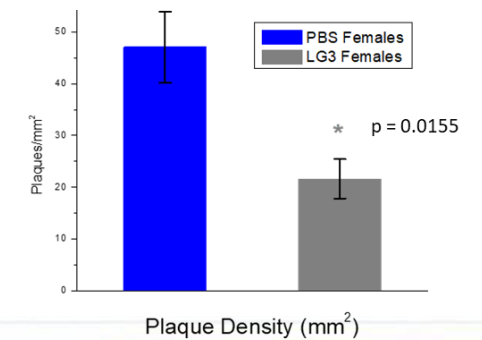
Hippocampus (Main site of AD pathology)



5XFAD Amyloid Model



Amyloid Protein Clearance (6E10) Immunofluorescence



rLG3 Treatment
Restores Neurovascular Health and Function



Restores pericyte coverage



Strengthens BBB integrity



Increases amyloid efflux



Reduces amyloid pathology



Supports cognitive function

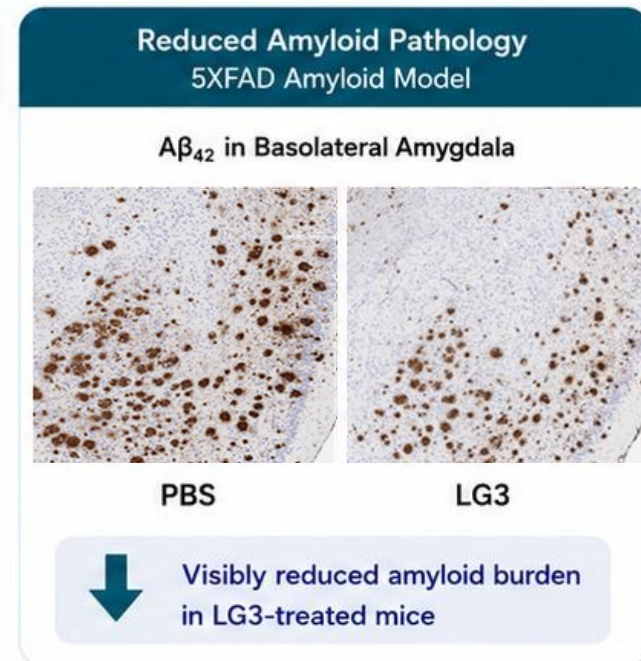
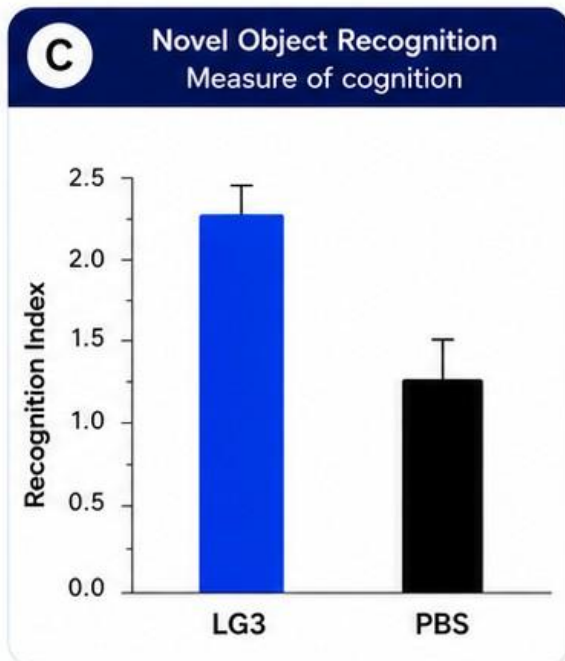
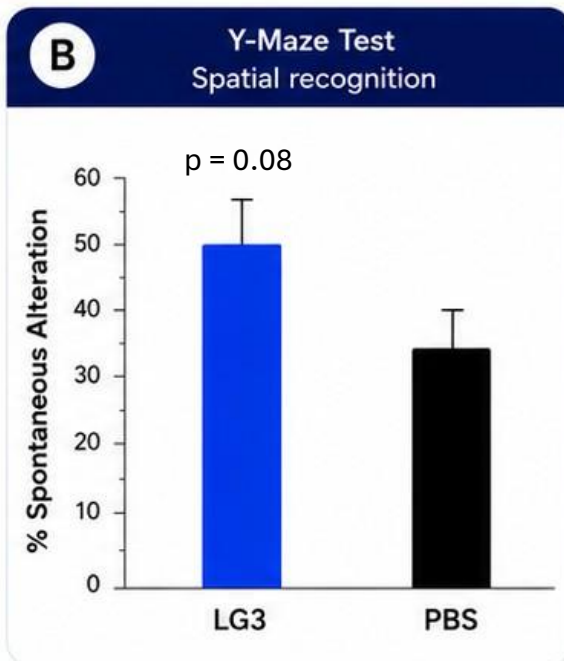
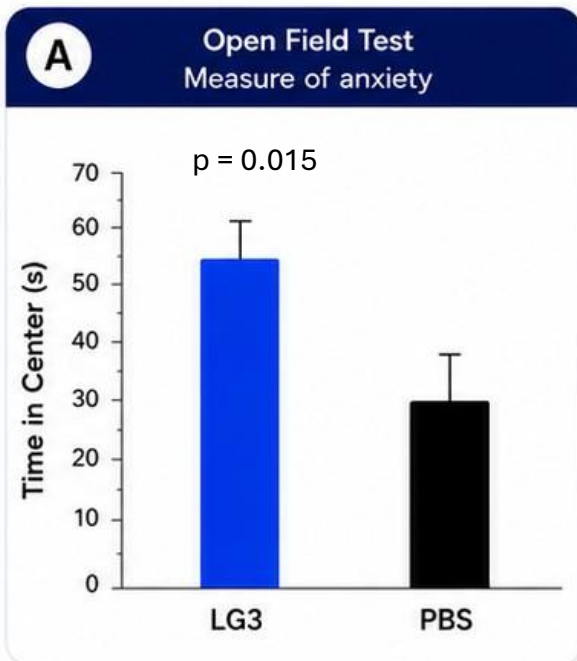


Broad neurovascular benefits with downstream impact

rLG3 Improves Cognitive Function in 5xFAD Mice



LG3 treatment significantly improved cognitive and emotional function across multiple behavioral domains, concurrent with **reduced amyloid burden in the basolateral amygdala.**



■ LG3 ■ PBS



LG3 increased time in the center of the arena, indicating reduced anxiety



LG3 improved spatial working memory as measured by Y-maze



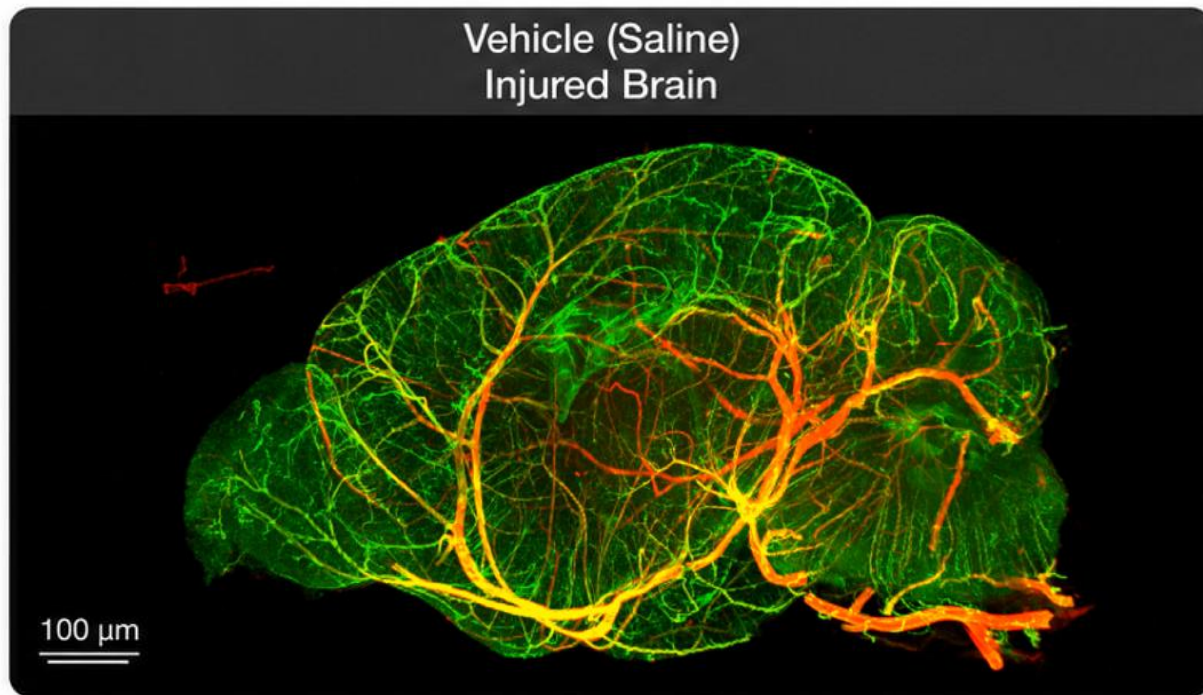
LG3 enhanced novel object recognition, indicating improved cognition



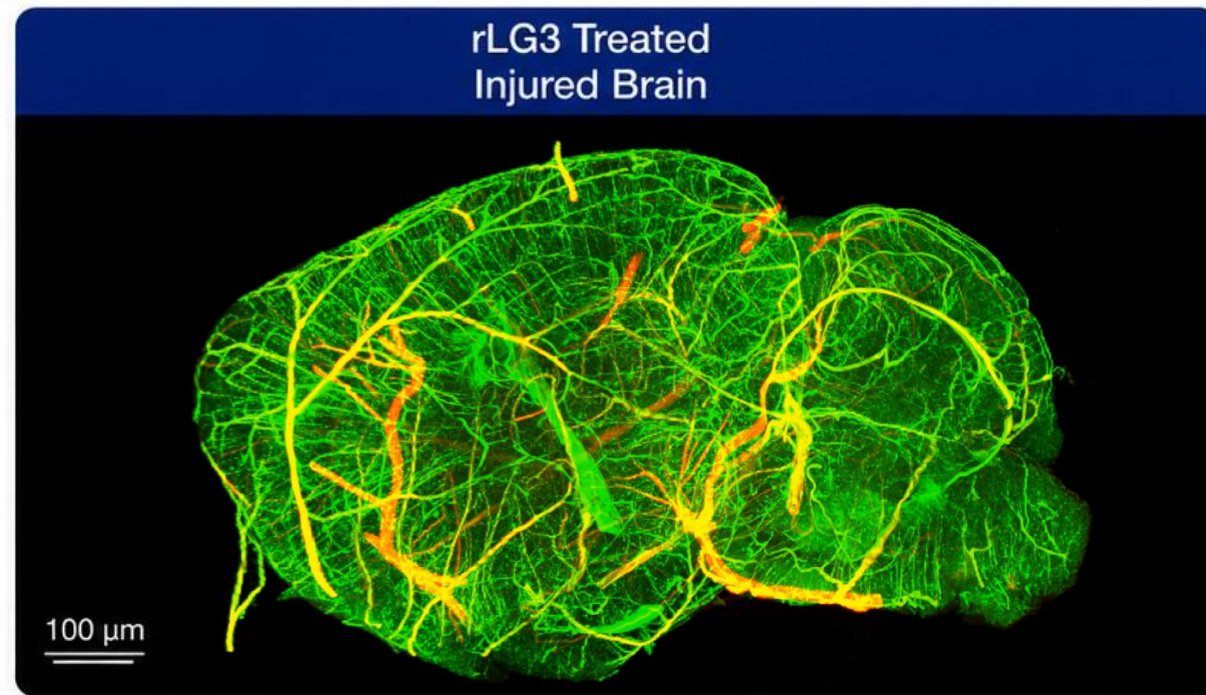
Improvements in behavior coincide with reduced amyloid burden in the basolateral amygdala

rLG3 Preserves Cerebrovascular Integrity

A single dose after reperfusion preserves microvascular structure and density.



Vessel Density: 8.25%
(57% loss vs. healthy tissue)



Vessel Density: 18.92%
(2% loss vs. healthy tissue)

Healthy Tissue Vessel Density: 19.19%







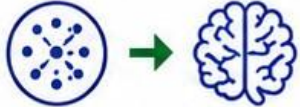
rLG3 treatment preserves cerebral microvascular architecture and density, supporting sustained blood flow and neurovascular function.

rLG3: A Multi-Mechanism, Disease-Modifying Therapeutic








Powerful Biology. Broad Potential. Clinic-Ready.

rLG3 PROPERTIES

-  **1** Profound Neuroprotection
-  **2** Eliminates tPA Hemorrhage Risk
-  **3** Restores the Blood Brain Barrier
-  **4** Reduces Biomarkers of CNS Injury
-  **5** Quickly crosses the BBB through Active Transport

CLINIC-READY

-  **Recombinant human protein**
Manufactured under cGMP
-  **High purity and batch consistency**
Robust analytical characterization and QC
-  **Favorable preclinical toxicology**
GLP studies complete
-  **Strong intellectual property position**
Composition and use of matter patents issued
-  **Clear path to first-in-human trials**
IND-enabling package in preparation

rLG3 Phase 1 Trial in Alzheimer's Disease Patients



Biomarker-Focused, Efficient Design to Establish Safety and Demonstrate Target Engagement



OUR FOCUS

Restore vascular integrity in Alzheimer's patients with baseline vascular abnormalities by MRI and fluid biomarkers.



OUR APPROACH

Advanced MRI technology measures vascular function at baseline and 48 hours after LG3 therapy to detect early restoration of vascular integrity.



WHERE WE CONDUCT THIS TRIAL

Leveraging advanced MRI at one of the premier clinical sites in the world.

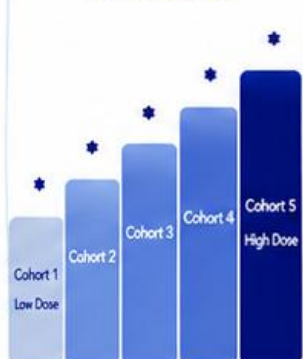


TRIAL SCHEMATIC

Randomized Placebo-Controlled Trial
(3:1 allocation LG3:placebo)

PART 1: SAD Single Ascending Dose

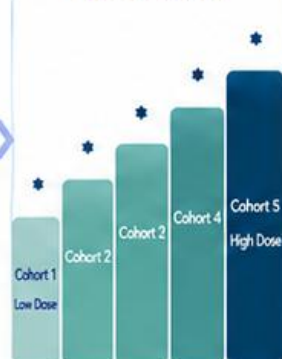
5 Dose Cohorts



- DSMB Review
- ✓ Safety
- ✓ Tolerability
- ✓ PK/PD
- ✓ Biomarkers

PART 2: MAD Multiple Ascending Dose

5 Dose Cohorts



~60 Participants
Alzheimer's Disease
screened for
patients with
baseline vascular
abnormalities by MRI
and fluid biomarkers

DOSING & IMAGING PLAN

SHORT, WELL-DEFINED EXPOSURE
3 intravenous doses over 6 days

Day 1



Day 3



Day 6



COMPREHENSIVE ASSESSMENTS

ADVANCED MRI
ASSESSMENTS
Measuring vascular
function



BASELINE
Pre-dose



48 HOURS
AFTER FINAL DOSE



BIOMARKER COLLECTION
Serum & CNS biomarkers



SERUM
Collected at
Baseline
and 48-hour
post-dose



CNS
Collected at
Baseline
and 48-hour
post-dose

Paired imaging and biomarker assessments
detect early restoration of vascular integrity

BIOMARKER READOUTS



VASCULAR (PRIMARY)

- DCE-MRI (Ktrans in hippocampus [BBB leakage])
- Cerebral Blood Flow (ASL MRI)
- Vascular reactivity



CNS INJURY (SECONDARY)

- Serum & CSF biomarkers:
• NfL, GFAP, sTREM2, YKL-40, pTau181, etc.



COGNITION (EXPLORATORY)

- ADAS-Cog13
- CDR-SB
- Memory & executive function tests

SAD = Single Ascending Dose

MAD = Multiple Ascending Dose

DCE-MRI = Dynamic Contrast-Enhanced MRI

ASL MRI = Arterial Spin Labeling MRI

MCI = Mild Cognitive Impairment

rLG3 Phase 1 Trial in Alzheimer's Disease Patients



Biomarker-focused, Efficient design. Clear path to target engagement.

A TRANSLATIONAL STUDY TO RESTORE VASCULAR INTEGRITY



OUR GOAL

Demonstrate early vascular target engagement and restoration of the neurovascular foundation in Alzheimer's disease.

TARGET RAISE

~\$12M

to execute a pioneering biomarker-focused Phase 1 trial designed to deliver high-information translational data with operational efficiency.

STUDY DESIGN



ADVANCED MRI IMAGING

DCE-MRI to assess BBB permeability and vascular reactivity



SERUM & CSF BIOMARKERS

Vascular, neuroinflammatory, and neurodegeneration markers



EXPLORATORY COGNITIVE MEASURES

Memory and executive function assessments



SAFETY & TOLERABILITY

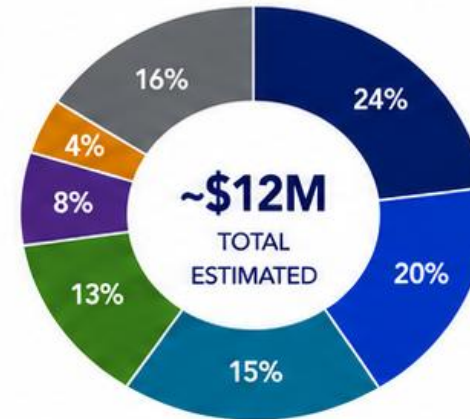
Continuous monitoring with focus on vascular safety and BBB



PRIMARY OBJECTIVE

Demonstrate target engagement and early restoration of vascular integrity.

ESTIMATED COST BREAKDOWN*



● Clinical Operations (Site & Patient Procedures)	~\$2.9M
● Imaging (DCE-MRI)	~\$2.4M
● Biomarkers (Serum & CSF)	~\$1.8M
● Manufacturing & CMC (Final Fill)	~\$1.6M
● Regulatory & Safety	~\$1.0M
● G&A / Contingency	~\$0.5M
● Other (Central Labs, Data Mgmt., Etc.)	~\$1.9M



Total Raise: ~\$12M

*Current estimates and may be subject to change.

WHY THIS STUDY MATTERS



UPSTREAM & MECHANISTIC

Addresses vascular pathology that drives cognitive decline upstream of neurodegeneration.



PRECISION BIOMARKER READOUTS

Designed to detect early and meaningful biological change in vascular integrity.



EFFICIENT & INFORMATIVE DESIGN

Focused design maximizes signal detection with rigorous, translational endpoints.



Biomarker readouts are designed to detect early restoration of vascular integrity and target engagement.

STUDY TIMELINE



1H 2027

Study Start-Up



1H 2028

Data Readout

rLG3: A Fundamental Solution for Age-Related Neurodegeneration

TURNING IRREVERSIBLE INTO RECOVERABLE

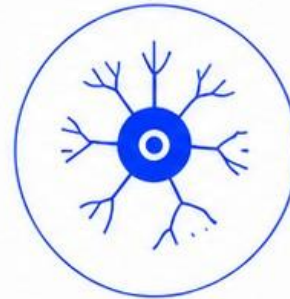


rLG3

A RECOMBINANT
BIOLOGICAL MOLECULE

DERIVED FROM AN
ENDOGENOUS
REPAIR PROTEIN

Harnessing the body's
natural repair pathway
to restore the brain from
the vascular injury.



RESTORES
neurovascular
integrity



REPAIRS
BBB
dysfunction



ENABLES
brain recovery
and resilience

A PROMISING PATH FORWARD

Upstream. Restorative. Clinical-ready.



Appendix

rLG3 Provides Potent Neuroprotection and Restores Function in Traumatic Brain Injury

Single-dose rLG3 reduces cell death, preserves brain tissue, and improves functional recovery.

KEY TAKEAWAYS



POTENT NEUROPROTECTION

Significant reduction in neuronal cell death in the cortex after TBI.



FUNCTIONAL RECOVERY

Rapid and sustained improvements in motor function and grip strength.



BBB INTEGRITY

Marked reduction of Evan's Blue leakage in the impact region.



SINGLE DOSE EFFICACY

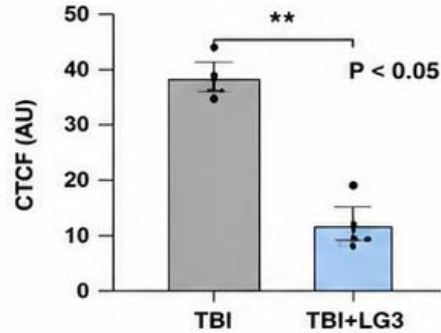
Robust benefits achieved with a single administration of rLG3.



These data demonstrate that rLG3 protects brain tissue and restores function after TBI by preserving vascular integrity and reducing secondary injury.

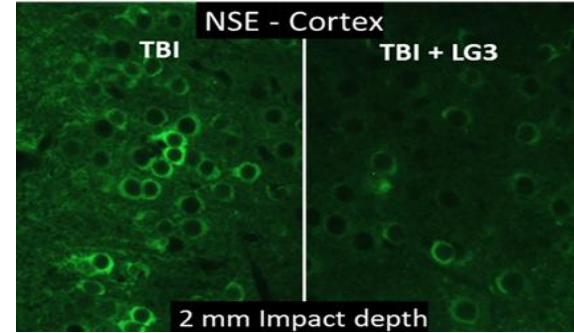
1 REDUCES CELL DEATH

Neuronal Cell Death (NSE)



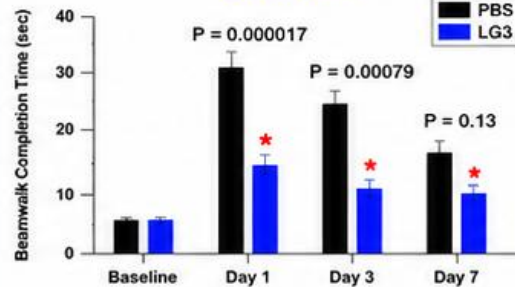
2 PRESERVES CORTICAL TISSUE

NSE – Cortex (Green Fluorescence)

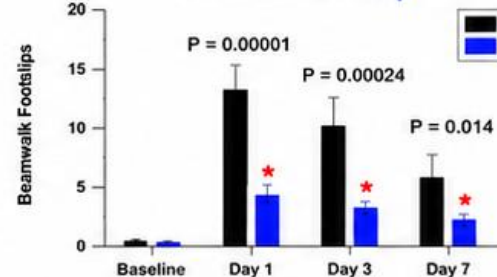


3 IMPROVES FUNCTIONAL PERFORMANCE

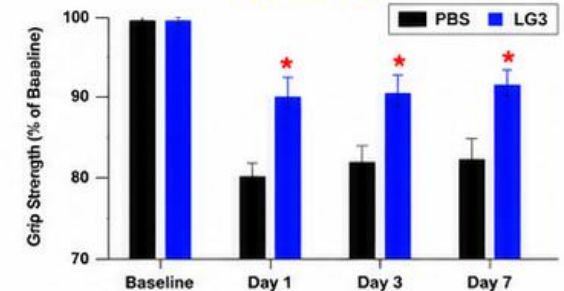
Beam Walk



Beamwalk: Footslips



Grip Strength



4 IMPROVES BBB INTEGRITY

Evan's Blue BBB Leakage (Impact Region)

TBI – Control (PBS)



TBI – LG3

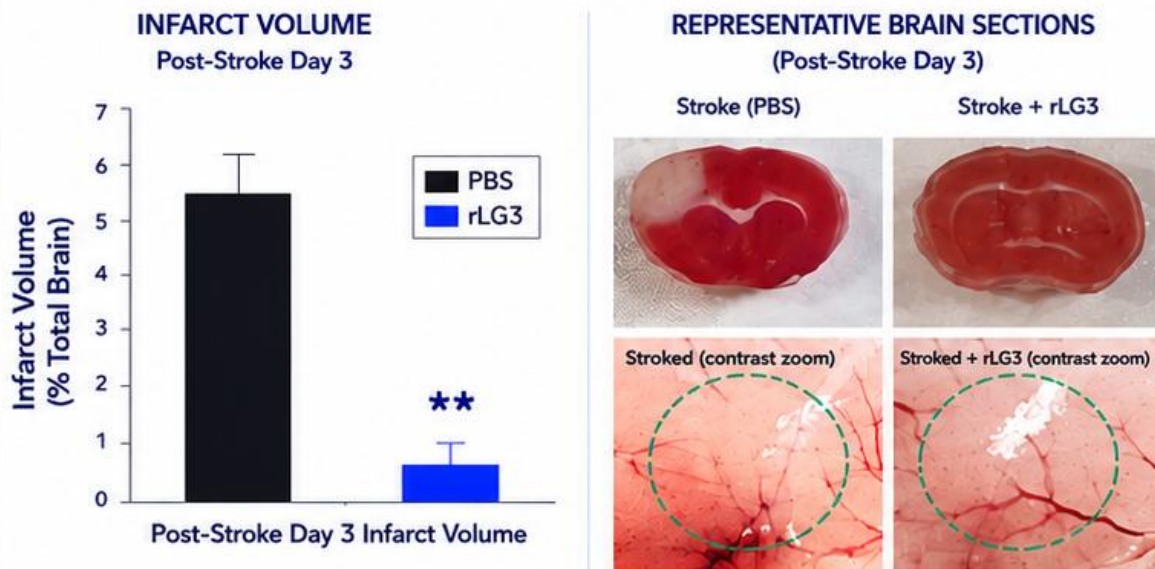


rLG3 Delivers Potent Neuroprotection and Eliminates tPA-Associated Hemorrhage

Restoring vascular integrity improves outcomes and broadens therapeutic potential.

1 ISCHEMIC STROKE MODEL (MCAO)

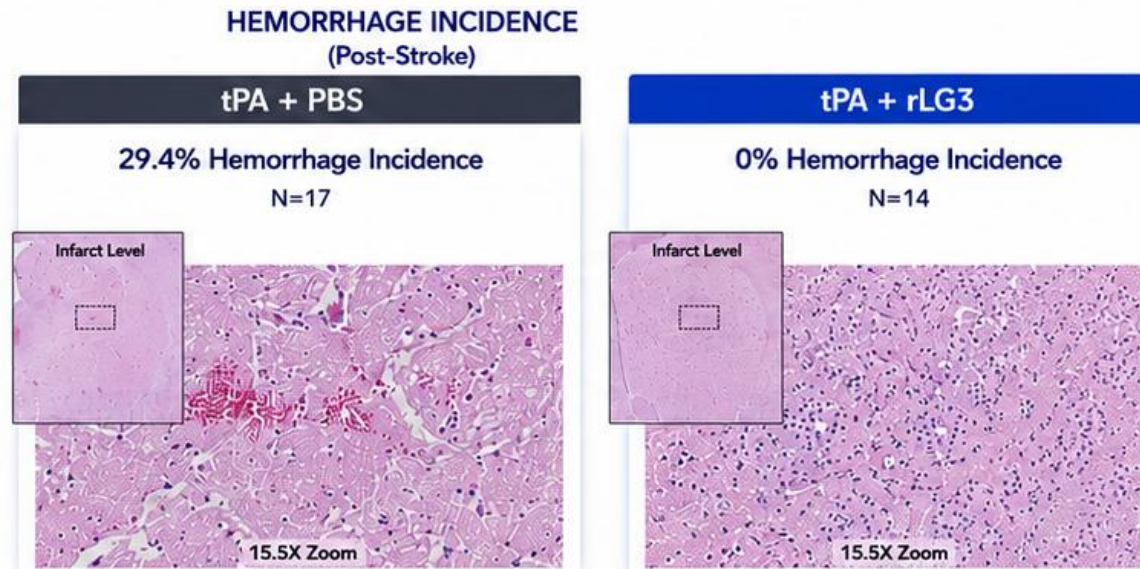
Profound Neuroprotection with Single Dose rLG3



rLG3 markedly reduces infarct volume and preserves brain tissue following ischemic stroke.

2 tPA MODEL OF ACUTE STROKE

rLG3 Eliminates tPA-Associated Hemorrhage



rLG3 completely prevents tPA-associated hemorrhage, supporting vascular protection and enabling safer reperfusion therapy.



Across ischemic stroke models, rLG3 protects brain tissue and preserves vascular integrity—supporting its potential as a disease-modifying therapy for stroke.

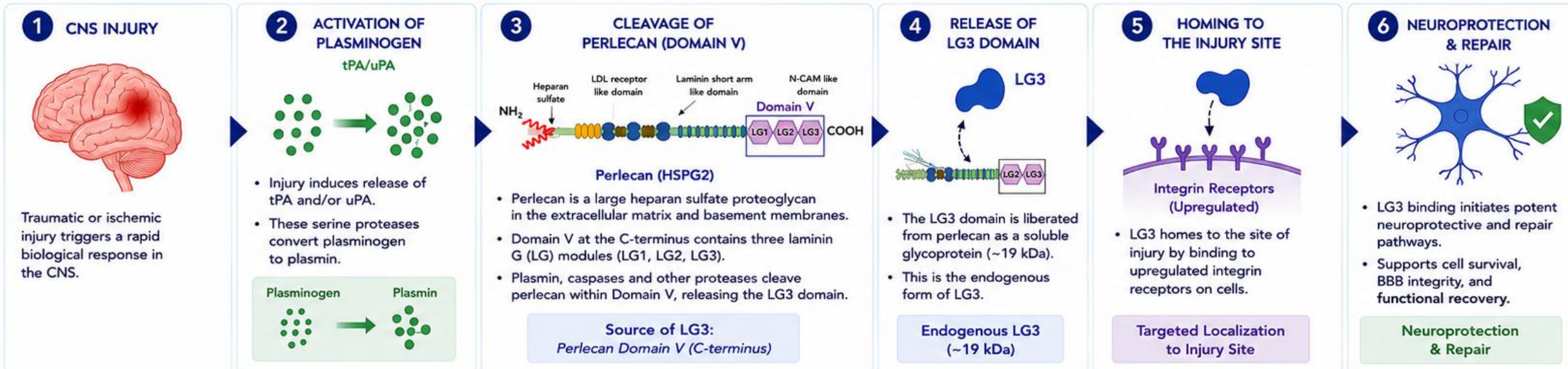
MCAO = middle cerebral artery occlusion; tPA = tissue plasminogen activator.

Biose et al., 2022. Translational Stroke Research; Stream internal data. Preclinical observations in young adult male mice (MCAO) and aged male and female rats (tPA), 60' MCAO, 90' tPA.

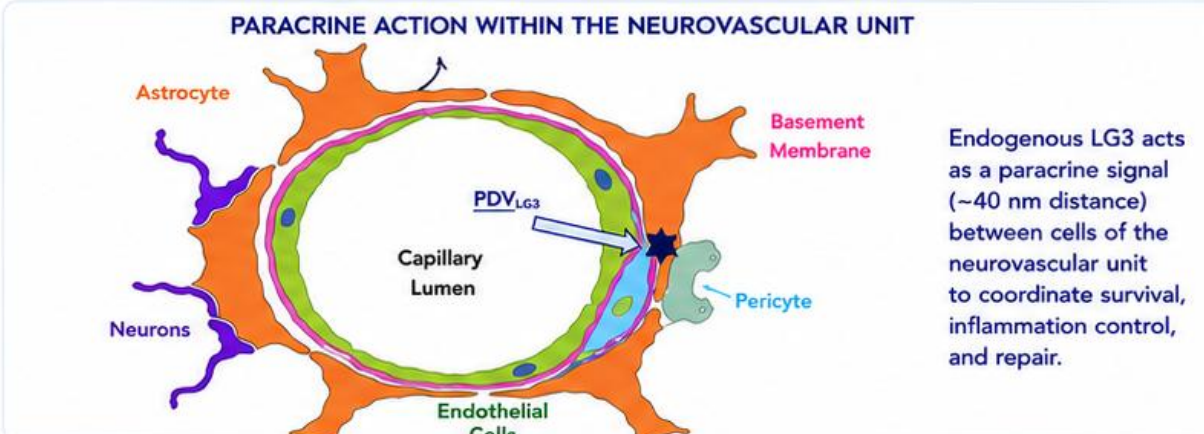
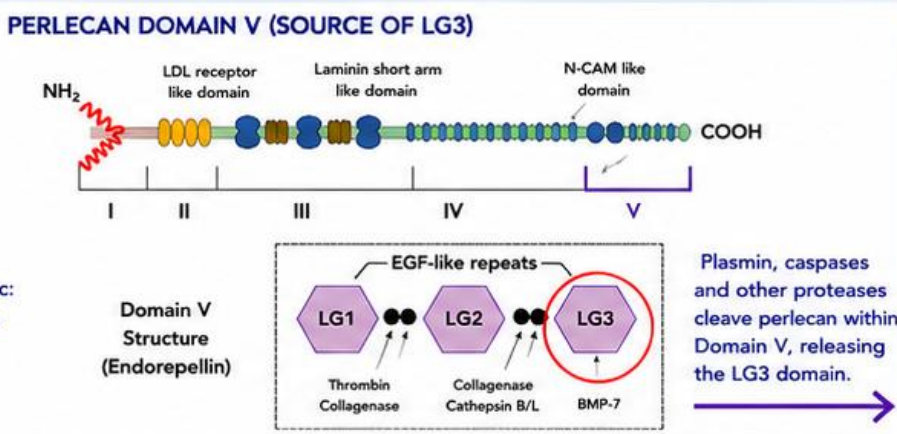
The Molecular Genesis of Endogenous LG3

A Conserved, Injury-Induced Response for Neuroprotection and Repair

Endogenous LG3 is generated through a tightly regulated, injury-induced proteolytic process that liberates the LG3 domain from Perlecan Domain V and delivers it to sites of CNS injury where it binds to cell surface integrin receptors to initiate neuroprotective and repair pathways.



- ~550 million years evolutionary conservation
- 21 kDa C-terminus of Perlecan Domain V
- Elevated in the brain of stroke and TBI patients
- Pleiotropic & anti-apoptotic; interacts with all cell types of the neurovascular unit (through integrin R's)



LG3 This is how endogenous LG3 is naturally generated and functions. *rLG3 therapeutically amplifies this intrinsic protective system.*